BMC Infectious Diseases

RESEARCH Open Access

Molecular epidemiology of *Escherichia coli* in bloodstream infections from a general hospital in Ningxia, China, 2022–2023

Xinxin Hu[1,3†], Jia Tao[1,2,3†], Lixin Yan[1,3], Wei Hong[1,3], Wen Wang[1,2,3], Liru Wang[1,2,3], Gang Li[1,2,3*] and Wei Jia[1,2,3*]

Abstract

Objective To analyse the antibiotic resistance, resistance genes and clonal relationship of *Escherichia coli* in bloodstream infections in Ningxia from 2022 to 2023.

Methods We retrospectively analyzed the antibiotic susceptibilities of 257 isolates. PCR was used to detect bla_{TEM}, bla_{SHV}, bla_{CTX-M}, *qnrS*, *qnrA*, *qnrB*, *oqxA*, *qepA*, *gyrA*, *gyrB*, *parC*, and *parE*, and the clonal relationship through multilocus sequence typing (MLST).

Results One hundred and twenty-nine of 257 patients were male (50.2%). The 257 *E. coli* isolates were mainly obtained from the Emergency, Hepatobiliary Surgery, and Haematology Departments, accounting for 56.6%, 7.3%, and 6.2%, respectively. There is no significant difference in sex and genes between the two groups over and under 60 years old ($P > 0.05$), but there is a significant difference in ST between them($P<0.05$). The antimicrobial susceptibility testing showed that the 257 isolates had the highest rates of resistance to ampicillin (82.8%), followed by cefazolin (71.6%), and all isolates were susceptible to tigecycline. Based on the antibiotic susceptibility results for ceftriaxone, we tested 126 isolates of *E. coli* for extended-spectrum beta-lactamase (ESBL) resistance genes. As a result, bla_{CTX-M} was detected in 76 isolates (60.32%), bla_{SHV} in 26 isolates (20.63%), and bla_{TEM} in 38 isolates (30.16%). Based on the ciprofloxacin and levofloxacin antibiotic susceptibility results, we tested for quinolone resistance genes in 148 isolates, revealing 66 isolates of *aac(6')-Ib-cr* (44.60%), 3 isolates of *oqxA* (2.02%), 32 isolates of *qnrS* (21.62%), and 2 isolates of *qepA* (1.35%). We did not detect *qnrA* or *qnrB*. The detection rates of *gyrA*, *gyrB*, *parC*, and *parE* were 98%, 42.6%, 91.2%, and 87.8%, respectively and the main amino acid mutations were Ser83 to Leu, Asp87 to Asn(75.2%), Leu417 to Ser, Ser418 to Leu (6.3%), Ser80 to Ile (65.2%), and Ser458 to Ala (21.5%), respectively. MLST revealed that the most common sequence types (STs) were ST69 (12.5%), ST131 (8.2%), and ST1193 (7.8%).

Conclusion In our hospital, *E. coli* was resistant to most commonly used antibiotics, and cefoperazone/sulbactam, cefotetan, amikacin, and tigecycline were empirically selected for the treatment of bloodstream infections. The

†Xinxin Hu and Jia Tao have made equal contributions.

*Correspondence:
Gang Li
ligang@nyfy.com.cn
Wei Jia
jiawei6365@126.com

Full list of author information is available at the end of the article

predominant ESBL genotype in our hospital was bla_{CTX-M} and the major quinolone resistance gene was *aac(6')-Ib-cr*. Clonal relationship analysis revealed genetic diversity among the isolates.

Keywords *Escherichia coli*, Bloodstream infection, Resistance genes, Antimicrobial susceptibility, Sequence type.

Introduction

Bloodstream infections are systemic illnesses caused by pathogenic microorganisms entering the bloodstream that threaten human life and health [1]. Bloodstream infections affect between 113 and 204 people for every 100,000 people worldwide. It can be caused by a variety of bacteria, including *Salmonella*, *Streptococcus*, *Enterococcus*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella*, *Pseudomonas aeruginosa*, *and* coagulase-negative staphylococci (CoNS). Among these, *E. coli* is the most frequently detected bacterium, followed by *S. aureus* and *P. aeruginosa* [2–6]. With the widespread use of antibiotics, the resistance of *E. coli* was gradually increasing and clinical treatment has become more challenging. Studies in China [7] and abroad [8] have shown that the bloodstream-infecting *E. coli* exhibit high resistance to ampicillin, ampicillin/sulbactam, and ciprofloxacin. β-lactams and fluoroquinolones are the primary antibiotics used to treat *E. coli* infections [9]. However, the resistance of *E. coli* to these antibiotics has increased in recent years.

The production of β-lactamase is the main mechanism by which *E. coli* develops resistance to β-lactams antibiotics and broad-spectrum β-lactamase is the most important for *E. coli* [10]. β-lactams antibiotics employ their unique quaternary amide molecules to act on the cell wall of bacteria, inhibiting the production of bacterial enzymes, reducing the binding ability of antibiotics, and lowering resistance. By acting on sites such as penicillin-binding protein 1 (PBP1) or PBP3, the target sites of bacterial and antibiotic interactions can be altered [11].

Quinolones are important broad-spectrum antibiotics used against gram-negative aerobic bacteria. Quinolones inhibit bacterial growth by suppressing DNA helicases and topoisomerases, thereby preventing bacterial protein synthesis [12]. Their resistance mechanism includes gene mutations in the quinolone resistance-determining region (QRDR) and plasmid-mediated quinolone resistance (PMQR) [13]. *E. coli* mainly develops resistance through amino acid mutations encoded by the *gyrA* and *parC* genes in the QRDR region [14], especially at positions 67–106 encoded by *gyrA*, and positions 71–110 encoded by *parC* [15–17]. Moreover, PMQR can undergo horizontal transfer between bacteria, leading to the spread of bacterial resistance [18, 19].

Xiao et al. [20] reported that, among 80 randomly selected isolates, 47 produced ESBLs; Sequencing of resistance genes identified $bla_{CTX-M-14}$, $bla_{CTX-M-15}$, and $bla_{CTX-M-27}$ as the most prevalent genotypes of ESBLs; ST131 was the most prevalent STs, followed by ST1193 and ST648. The characteristics of bacterial strains, antibiotic resistance, and resistance mechanisms vary in different regions, and these differences have not been recorded in Ningxia, China. To provide a reference for the treatment of clinical bloodstream infections and the control of antibiotic resistance, we conducted a retrospective study on the antibiotic resistance of *E. coli* in bloodstream infections in Ningxia, China from 2022 to 2023 and also conducted molecular epidemiological and studied the ESBL and quinolone resistance genes, sequence types, and antibiotic resistance rates.

Materials and methods

Bacterial strains and clinical data collection

Between February 2022 and July 2023, 257 *E. coli* isolates from blood cultures were collected from Ningxia Medical University. The clinical data of 257 patients were obtained from electronic medical records, including demographic information (sex, age, and department) and signs of infection (white blood cell count and percentage, c-reactive protein, and procalcitonin). Sex, resistance genes and ST were compared between patients over and under 60 years of age to analyze factors associated with bloodstream infections.

Strain identification and antibiotic susceptibility test

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was used for species identification. The VITEK® 2 automatic system was used for the antimicrobial susceptibility test. Two cards, ZN09 and N335, were used for *Escherichia coli*. The quality control strain was *Escherichia coli* ATCC 25,922. The antibiotics include ampicillin, cefoperazone/sulbactam, sulbactam/ampicillin, tazobactam/piperacillin, cefazolin, cefuroxime, ceftazidime, ceftriaxone, cefepime, cefotetan, aztreonam, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, levofloxacin, sulfamethoxazole, minocycline, and tigecycline.

Resistance genes detection and MLST

DNA was extracted by boiling method. Xi'an Sheng Gong Biological Company (Shanxi Province, China) synthesized the resistance gene primers according to pertinent literatures [21, 22] (Supplementary Table S1). The amplification system of the gene was set up as follows (total volume, 50 μL): 25 μL of 2× HieffTM PCR Master Mix, 21 μL of dd H_2O, 1 μL of forward primer and 1 μL of reverse primer, 2 μL of DNA template. Based on the antibiotic susceptibility results of ceftriaxone, β-lactam

antibiotic resistance genes, such as bla_{TEM}, bla_{CTX-M}, and bla_{SHV}, were examined in 126 *E. coli* isolates. Similarly, based on the ciprofloxacin and levofloxacin antibiotic susceptibility results, the quinolone resistance genes of 148 isolates of *E. coli*, including *aac(6')-Ib-cr*, *oqxA*, *qepA*, *qnrS*, *qnrA*, *qnrB*, *gyrA*, *gyrB*, *parC*, and *parE* were examined. The positive amplification products were sent to Xian BGI Technology Co. for Sanger sequencing. Nucleotide sequences (bla_{TEM}, bla_{CTX-M}, bla_{SHV}, *aac(6')-Ib-cr*, *oqxA*, *qepA*, *qnrS*, *qnrA*, *qnrB*) were compared by BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi). To detect the mutations, we compared *gyrA*, *gyrB*, *parC*, and *parE* sequences with those of the wild-type *E. coli* K-12 (NCBI serial number NC-000913.3) sequence.

MLST was used to determine the STs of the isolates and seven *E. coli* housekeeping genes were amplified by standard PCR protocol (https://enterobase.readthedocs.io/en/latest/mlst/mlst-legacy-info-ecoli.html) (Supplementary Table S2). The MLST results were compared with the ST results using https://pubmlst.org/bigsdb?db=pubmlst_mlst_seqdef and an evolutionary tree was created using GrapeTree.

Statistical methods

WHONET 5.6 software was used to analyze the patient's age, sex, departmental distribution, and antibiotic susceptibility. Statistical software SPSS 26.0 was used for data processing. Sex, resistance genes and ST were compared between patients over and under 60 years of age to analyze the related factors of bloodstream infections. The chi-square test was used to analyze the counting data. Continuous correction is applied when the theoretical frequency is less than five. When the frequency of each cell is less than 1, Fisher's exact probability method is used. The statistically significant difference was defined as $P<0.05$. The mean ± standard deviation is used for measurement data that have a normal distribution, and the two independent samples t-test is used for representation if analysis of variance shows that the variances are homogeneous. The corrected t-test is employed for representation in cases where the variances are not homogeneous.

Results

Strain clinical information

A total of 257 *E. coli* isolates were collected from patients with bloodstream infections. Among the 257 patients, 129 were male (50.2%), ranging in age from 4 months to 97 years old (mean: 61 years old). The included patients in this study were mainly from the Emergency Department (145, 56.6%), the Hepatobiliary Surgery department (19, 7.3%), and the Hematology department (16, 6.2%) (Fig. 1). Statistical analysis of the test results of the 257 patients revealed that 31.1% had elevated C-reactive protein levels, 91% had elevated procalcitonin levels, 54.5% had elevated white blood cells and neutrophil counts, and 4.7% had normal white blood cells and elevated neutrophil counts. Additionally, 32% of patients presented with other infections, such as abdominal infections. The statistical results show that there is no significant difference in sex and genes between the two groups over and under 60 years old ($P>0.05$), but there is a significant difference in ST between them($P<0.05$). There is a significant difference between the two age groups (45.84 ± 13.23 VS 73.17 ± 8.08 t=-20.35 $P=0.00$). as detailed in Supplementary Table S3.

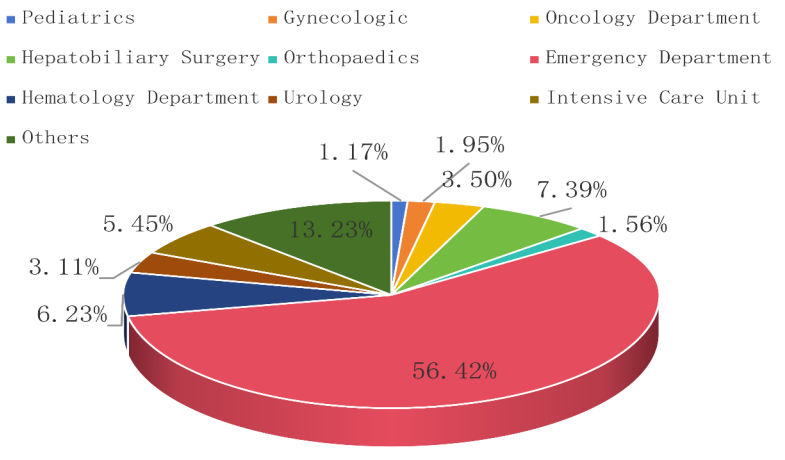

Fig. 1 Distribution of 257 *Escherichia coli* isolates according to their departments

Table 1 Antimicrobial susceptibility of 257 *Escherichia coli* isolates

Antibiotics	Number	Resistance rate(%)
AMP	256	82.8
CSL	256	2
SAM	257	36.2
TZP	257	2.3
CZO	257	71.6
CXM	257	51.8
CAZ	257	27.6
CRO	257	52.5
FEP	257	7.8
CTT	257	0.8
ATM	257	32.7
IPM	257	0.4
MEM	257	0.4
AMK	257	1.2
GEN	257	32.3
CIP	257	48.2
LVX	257	47.5
SMZ-TMP	257	49
MNO	256	16
TGC	256	0

AMP: ampicillin, CSL: cefoperazone/sulbactam, SAM: sulbactam/ampicillin, TZP: tazobactam/piperacillin, CZO: cefazolin, CXM: cefuroxime, CAZ: ceftazidime, CRO: ceftriaxone, FEP: cefepime, CTT: cefotetan, ATM: aztreonam, IPM: imipenem, MEM: meropenem, AMK: amikacin, GEN: gentamicin, CIP: ciprofloxacin, LVX: levofloxacin, SMZ-TMP: sulfamethoxazole-trimethoprim, MNO: minocycline, TGC: tigecycline

Antibiotic susceptibility testing

According to the breakpoint criteria mentioned in the Clinical and Laboratory Standards Institute 2022 guideline [23]. The resistance rates to cephalosporin antibiotics such as cefazolin, ceftriaxone, and cefuroxime were high, accounting for 71.6%, 52.5%, and 51.8%, respectively; the resistance rate to ampicillin was 82.8%, and most isolates (>99%) were susceptible to meropenem, imipenem and cefotetan. The resistance rate to aminoglycoside antibiotics, such as amikacin, was relatively low (1.2%), whereas that to gentamicin was relatively high (32.3%). The resistance rates to quinolones, such as ciprofloxacin and levofloxacin, were relatively high at 48.2% and 47.5%, respectively. All isolates were susceptible to tigecycline(Table 1).

Resistance genes

One hundred and twenty-six *E. coli* isolates were screened for extended-spectrum β-lactamase resistance genes, including bla_{SHV}, bla_{TEM}, and bla_{CTX-M}, in accordance with the antibiotic susceptibility results of ceftriaxone. The detection rates of bla_{SHV}, bla_{TEM}, and bla_{CTX-M} were 20.6%, 30.2%, and 60.3%, respectively (Fig. 2). Based on the ciprofloxacin and levofloxacin antibiotic susceptibility results, 148 isolates were tested for quinolone resistance genes including *aac(6')-Ib-cr* ($n=66$), *oqxA* ($n=3$), *qepA* ($n=2$), and *qnrS* ($n=32$), but no *qnrA* nor

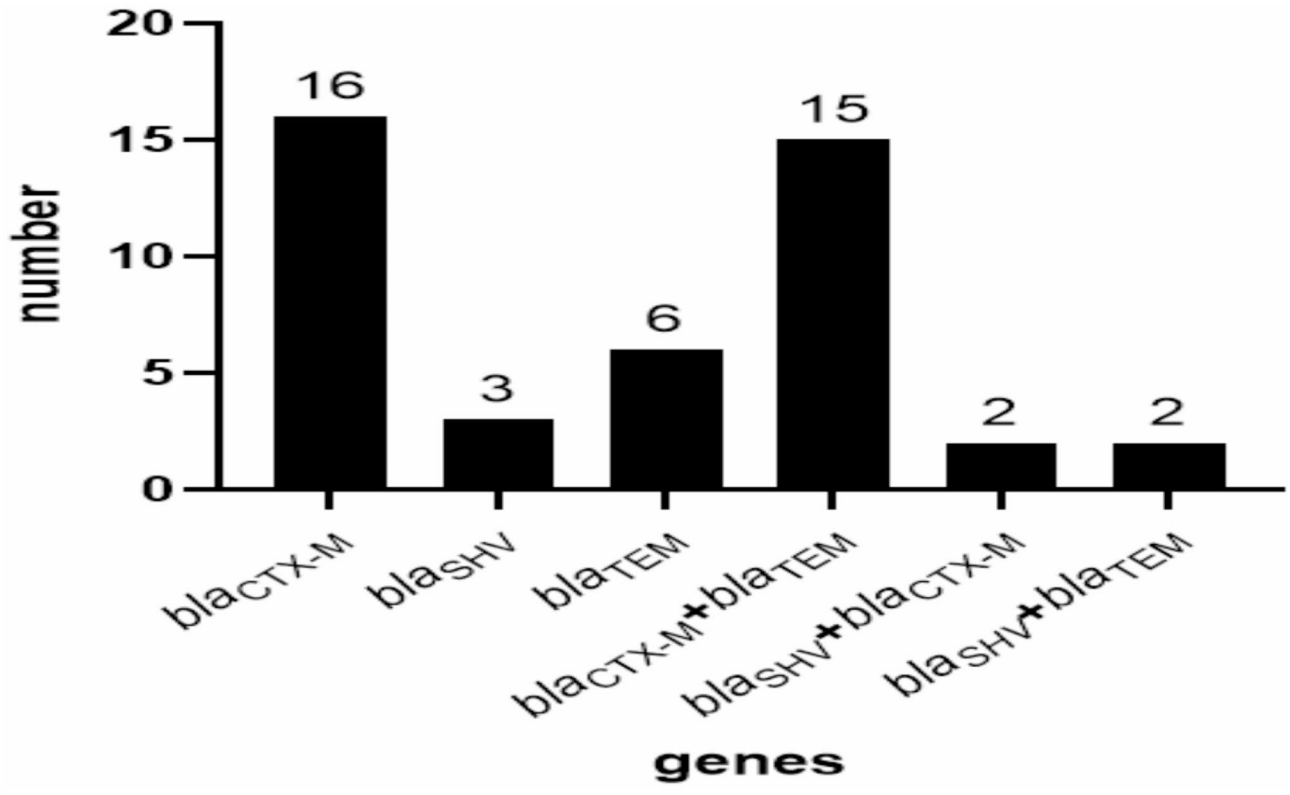

Fig. 2 Detection of extended-spectrum β-lactamase genes in 120 isolates of *Escherichia coli*

qnrB were found (Fig. 3). We identified many combinations of ESBL and quinolone resistance genes, of which bla_{CTX-M}+*aac(6')-Ib-cr* (11 isolates) was the most common. Further details are provided in Supplementary Table S4. The detection rates of *gyrA*, *gyrB*, *par*C, and *parE* were 98%, 42.6%, 91.2%, and 87.8%, respectively and the main amino acid mutations were Ser83 to Leu and Asp87 to Asn(75.2%), Leu417 to Ser and Ser418 to Leu(6.3%), Ser80 to Ile (65.2%), and Ser458 to Ala(21.5%) (Supplementary Table S5). Based on the different combinations of amino acid mutations, we identified 27 types of mutations, among which Ser83 to Leu, Asp87 to Asn in *gyrA*, Ser80 to Ile in *parC* (45 isolates) were the main mutation types, followed by Ser83 to Leu, Asp87 to Asn in *gyrA*, Ser80 to Ile, Glu84 to Val in *parC*, (26 isolates). The proportion of other combinations was relatively small, as shown in Supplementary Table S6. Of the 157 isolates that were resistant to ciprofloxacin, 75.8% had mutations in *gyrA* and *parC* and 68.8% of the isolates had MIC ≥ 4 μg/ml.

MLST analysis

According to the MLST results, 257 isolates of *E. coli* were divided into 68 STs, of which the top ten were ST69 (32/257, 12.5%), ST131 (21/257, 8.2%), ST1193 (20/257, 7.8%), ST73 (10/257, 3.9%), ST95 (10/257, 3.9%), ST13381 (8/257, 3.1%), ST10 (9/257, 3.5%), ST38 (6/257, 2.3%), ST648 (4/257, 1.6%), and ST44 (5/257, 2%). The other STs accounted for a smaller percentage of the total population (Supplementary Table S7). We constructed a phylogenetic tree based on the ST using GrapeTree (Fig. 4) and summarized STs, resistance genes, and antibiotic resistance profiles. We found that different STs (except ST5295, and ST127) carried ESBL and quinolone resistance genes and had varying degrees of resistance to β-lactams, quinolones, aminoglycosides, and other antibiotics, as shown in Supplementary Table S7.

Discussion

Bloodstream infection is an infectious illness with a high morbidity and death rate, an abrupt start, and a fast disease course advancement. *E. coli* was the most common cause of bloodstream infections (BSI) in China, accounting for 22.2% of BSI pathogens, according to data from the China Antimicrobial Surveillance Programme. Given the limited studies on bloodstream infections in this area, we sought to examine the clonal analysis, antibiotic susceptibility, and resistance genes of bloodstream-infecting *E. coli* strains in the Ningxia region between February 2022 and July 2023 to guide and establish a foundation for bloodstream infection treatment.

Due to weakened immunity, poor nutrition, and the prevalence of basic diseases like diabetes and hypertension, the incidence of bloodstream infection is higher in the elderly than in young adults [24]. In this study, we defined people over 60 years old as elderly, with 141 people being elderly, accounting for 54.9%. Statistical analysis revealed that the age difference between the two groups was statistically significant. Research [25] has indicated that the incidence and severity of bloodstream infections vary by sex. There is currently little population-based research, and comparing two groups is pointless. There was no statistical difference in the detection of resistance genes among different age groups in this study. The two groups' differences in ST are statistically significant, suggesting that ST is a risk factor for bloodstream infections.

Our results revealed that *E. coli* causing bloodstream infection is susceptible to carbapenem antibiotics, such as imipenem (0.4% resistant) and meropenem (0.4% resistant), but resistant to ampicillin (82.8%), cefazolin (71.6%), ceftriaxone (52.5%), and other β-lactam antibiotics. The resistance rates of *E. coli* to quinolone antibiotics, such as ciprofloxacin and levofloxacin, were 48.2% and 47.5%, respectively. The resistance rate to aminoglycoside antibiotics, such as amikacin, was relatively low (1.2%), but slightly higher than that of gentamicin (32.3%). These data are consistent with the antibacterial antibiotic monitoring data in China for 2022 and 2023 (https://www.chinets.com/Data/AntibioticDrugFast).

ESBLs are β-lactamase that can hydrolyze penicillin, cephalosporin, and monocyclic antibiotics, causing bacteria to develop resistance to various β-lactam antibiotics [26]. ESBL-positive *E. coli* uses plasmid conjugation, transfer, and transmission to spread resistance genes and can accumulate a series of resistance gene clusters through these pathways. This phenomenon is called "polygenic resistance aggregation," and can result in species exhibiting multiple resistance phenotypes [27].

Currently, bla_{TEM}, bla_{SHV}, bla_{CTX-M}, and bla_{OXA}, are the most prevalent genotypes of ESBLs [28], among which the bla_{CTX-M} is the most common in China [29–31]. Among the three ESBL genotypes identified in this study, 76 isolates of bla_{CTX-M} were detected. More than half of the isolates carried the ESBL gene, which may be one of the reasons for the high resistance of our bacteria to β-lactam antibiotics such as cefazolin and ampicillin.

Quinolones are a type of synthetic antimicrobial medication that is frequently used to treat and prevent infections caused by mycoplasma as well as gram-positive and gram-negative bacteria. The main reason for *E. coli* resistance to quinolone antibiotics is mutations in the QRDR gene, especially in the amino acid positions 67–106 encoded by the *gyrA* gene and the amino acid positions 71–110 encoded by the *parC* gene. The PMQR genes induce low quinolone resistance in *E. coli* [32]. In our study, among 157 isolates resistant to ciprofloxacin, 68 isolates had mutations in *gyrA* (Ser83 to Leu, Asp87

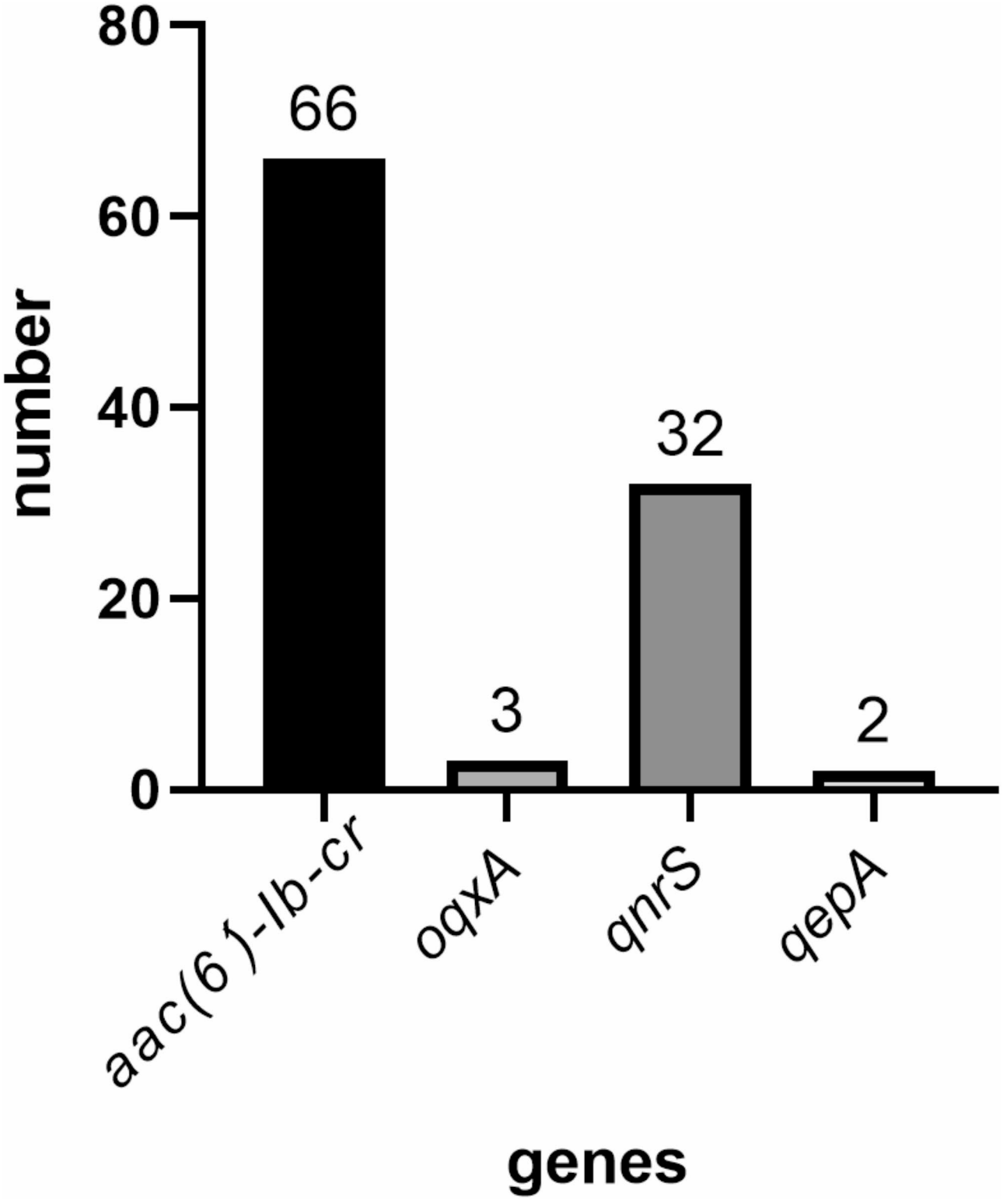

Fig. 3 Detection of quinolone resistance genes in 150 isolates of *Escherichia coli*

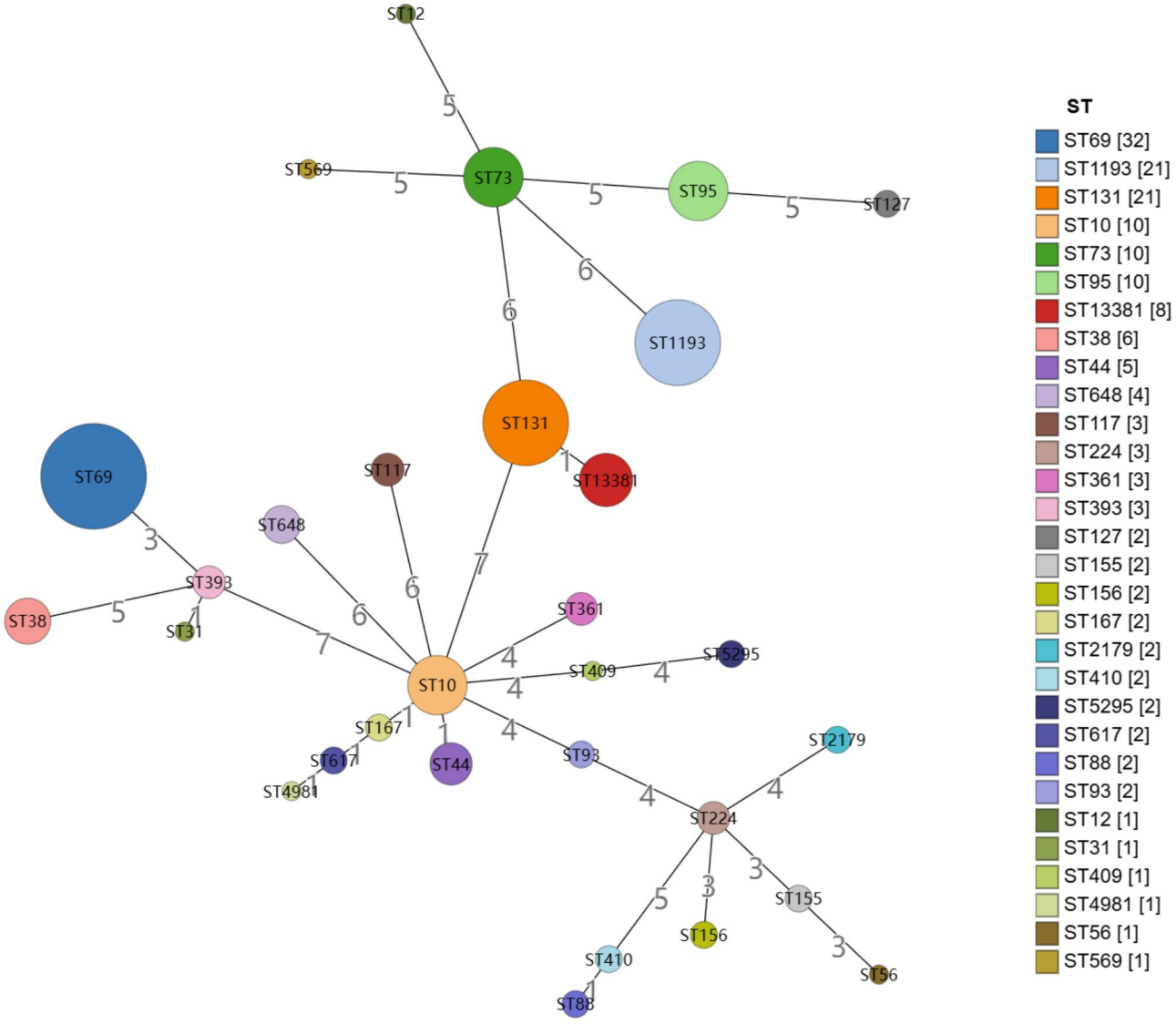

Fig. 4 GrapeTree software to construct a phylogenetic tree for *Escherichia coli*

to Asn) and *parC* (Ser80 to Ile) and 98.5% (67/68) isolates had a minimum inhibitory concentration ≥ 4 μg/ml.

The aminoglycoside acetyltransferase gene, *aac(6')-Ib-cr*, which produces a protein capable of altering quinolones to generate resistance, is basically a variation of the common plasmid-mediated aminoglycoside resistance gene, *aac(6')-Ib* [33]. In our study, 44.6% of *E. coli* carried *aac(6')-Ib-cr*, representing the highest detection rate. *aac(6')-Ib-cr* can also modify ciprofloxacin and norfloxacin and is frequently carried by bla_{CTX-M} isolates, conferring low-level resistance to amikacin with MICs that do not exceed resistance breakpoints [34]. In this study, 21 out of 66 *aac(6')-Ib-cr* genes simultaneously carried the $bla_{\mathrm{CTX-M}}$ gene. All 66 isolates were susceptible to amikacin and had MICs < 16 μg/ml.

Other quinolone resistance genes are the *qnr* genes, which spread horizontally among bacteria, cause widespread outbreaks, and can co-integrate with other resistance genes, such as bla_{SHV}, $bla_{\mathrm{CTX-M}}$, $bla_{\mathrm{VEB-1}}$, $bla_{\mathrm{FOX-5}}$, and $bla_{\mathrm{DHA-1}}$ making clinical treatment more difficult [35, 36]. According to reports [37], one-third to two-thirds of Enterobacteriaceae bacteria that produce ESBL are also resistant to fluoroquinolones. A total of 32 *qnrS*-positive isolates were detected in this study, of which 34.4% carried both ESBLs and *qnrS* resistance genes; however, we did not detect *qnrA* or *qnrB*. Thirty-two *qnrS*-positive isolates showed resistance to ciprofloxacin, with a resistance rate of 90.6% to levofloxacin.

Carbapenem antibiotics are atypical β-lactam antibiotics with the widest spectrum and strongest antibacterial activity [38, 39]. Due to their stability against β-lactamase

and low toxicity, they emerged as the most important antibiotics for treating severe bacterial infections. Meropenem and imipenem are carbapenem antibiotics that inhibit the cross-linking of peptidoglycans during cell wall synthesis by inactivating penicillin-binding proteins, ultimately leading to the osmotic lysis of bacterial cells [40, 41]. In this study, only one isolate was resistant to meropenem and imipenem, while all other isolates were susceptible. The main mechanisms of Enterobacteriaceae to be resistant to carbapenem antibiotics include the production of carbapenemases, hyper-production of AmpC enzymes, or ESBLs combined with loss of outer membrane porins and/or high expression of efflux pumps [42–44]. Of these, carbapenemases are the most important because their coding genes are mostly located on transferable elements such as plasmids or transposons, which can spread between different bacterial genera [45]. We will conduct more in-depth research on this isolate in the future.

As a chemically modified product of minocycline, tigecycline is a semi-synthetic antibiotic of glycylcyclines used for injection. Tigecycline belongs to the third generation of new tetracycline antibiotics and has ultra broad-spectrum antibacterial activity, with a similar structure and mechanism of action to tetracycline. Tigecycline is used to treat infectious diseases caused by multi-antibiotic-resistant pathogens [46]. It inhibits bacterial protein synthesis by binding to the ribosomal 30S subunit and prevents aminoacylated tRNA molecules from entering the ribosomal A site [47]. In our study, all isolates were susceptible to tigecycline.

MLST typing and phylogenetic analyses revealed genetic diversity among *E. coli* causing bloodstream infections. We identified 68 STs that were relatively dispersed. This could be attributed to the fact that more than half of our blood culture specimens were from the Emergency Department and patients were from different regions. ST69 was the most prevalent in our study (12.5%), followed by ST131 (8.2%), and ST1193 (7.8%). Lipworth et al. reported [48] that, over a 10-year period, the STs of bloodstream infections of *E. coli* were mainly stable by ST73, ST131, ST95, and ST69. Paramita et al. showed [49] that from total of 22 *E. coli* isolates, 12 different STs were identified, of which ST131, ST69, ST38, and ST405 accounted for 63.6%. There were 19 isolates carrying β-lactamase resistance genes, among which 27.3% isolates carried $bla_{\text{CTX-M-15}}$, and 22.7% carried $bla_{\text{CTX-M-27}}$. *aac (6')-Ib-cr* was detected in 3 isolates (13.6%). There were certain common STs of *E. coli* with bloodstream infections in different regions, especially ST131 with varying degrees of prevalence worldwide.

E. coli ST131, the major extraintestinal pathogenic *E. coli* [50], is an important human pathogen that is prevalent worldwide. This strain typically carries resistance genes for broad-spectrum cephalosporins and fluoroquinolones, and the ST131 strain exhibited higher virulence characteristics than other clinical fluoroquinolone-resistant/ESBL-producing strains [51]. The significant increase in the number of ESBL-producing *E. coli* may be associated with clonal amplification of ST131 [52]. While ST69 strains had minimal ESBLs and quinolone resistance genes, 62% of all ST131 strains in our study carried ESBL resistance genes, and 42.86% of these strains carried quinolone resistance genes. Additionally, in line with earlier findings, we discovered that ST131 had a high rate of resistance to cefuroxime, ceftazidime, ceftriaxone, amikacin, ciprofloxacin, and levofloxacin; however, ST69 had a low incidence of resistance to these antibiotics [53]. The resistance rate of ST131 isolates to cephalosporins, aminoglycosides, fluoroquinolones, and other antibiotics reported in the literature was significantly higher than that of other ST strains [54]. This may be attributed to the fact that ST131 carried a relatively large number of ESBL-resistance genes and that different STs exhibited differences in their susceptibility to antibiotics. In addition, analysis of the quinolone resistance-determining regions revealed point mutations leading to double mutations in *gyrA* (Ser83 to Leu and Asp87 to Asn) and *parC* (Ser80 to Ilea and Glu84 to Val) or double mutations in *gyrA* (Ser83 to Leu) and *parC* (Ser80 to Ile), suggesting that *E. coli* ST131 has a high level of fluoroquinolone resistance.

ST1193 *E. coli* is a multiantibiotic-resistant bacterium that causes a wide range of infections [55], with resistance to quinolones being one of its main features [56]. In our study, 50% of the ST1193 isolates carried quinolone resistance genes, and the antibiotic susceptibility results showed that all ST1193 isolates were 100% resistant to ciprofloxacin and levofloxacin, whereas they were not resistant to cefuroxime, cefotetan, tigecycline, imipenem, or meropenem.

Conclusion

In conclusion, the epidemic resistance gene for ESBL production in bloodstream-infecting *E. coli* in the Ningxia region from 2022 to 2023 was $bla_{\text{CTX-M}}$. The *aac (6')-Ib-cr* gene was the dominant quinolone resistance gene, and some isolates carried multiple resistance genes simultaneously. The double mutations of *gyrA* (Ser83 to Leu and Asp87 to Asn) and *parC* (Ser80 to Ile) were the main cause of the resistance of *E. coli* to quinolones. There is no significant difference in sex and genes between the two groups over and under 60 years old ($P>0.05$), but there is a significant difference in ST between them($P<0.05$). ST131 and ST69 were prevalent in Ningxia, with some differences in the resistance genes carried and resistance rates with different STs. By analyzing the antibiotic susceptibility, antibiotic-resistant genes, and clonal analysis of *E. coli* from bloodstream infections

in our hospital, we suggest that clinicians empirically use antibiotics such as tigecycline, amikacin, or second-generation or third-generation cephalosporins such as cefoperazone/sulbactam and cefotetan (cephamycin) to treat bloodstream infections caused by *E. coli* to prevent further spread of multidrug-resistant bacteria and improve prevention, control, and monitoring capabilities.

Limitations of the study

We conducted a retrospective study on the molecular epidemiology of bloodstream infections caused by *E. coli* from 2022 to 2023. Some antibiotics, such as colistin, were not included in the antibiotic susceptibility testing. In this study, the number of *E. coli* isolates we investigated was relatively small. However, our research can improve the molecular epidemiological data of bloodstream infections caused by *E. coli* in the Ningxia region, provide medication guidance for clinical use, and provide theoretical basis for hospital infection prevention and control.

Abbreviations

MLST	Multilocus sequence typing
ESBL	Extended spectrum Beta-Lactamase
ST	Sequence type
E. coli	*Escherichia coli*
S. aureus	*Staphylococcus aureus*
P. aeruginosa	*Pseudomonas aeruginosa*
CoNS	Coagulase-negative staphylococci
CLSI	Clinical and Laboratory Standards Institute
BSI	Bloodstream infections

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-10658-3.

Supplementary Material 1

Acknowledgements

The authors would like to thank the participating investigators of the study.

Author contributions

W J, G L, J T: study design. J T: Article writing. LR W, W W: data collation. XX H, LX Y, W H: statistical analysis. All authors read and approved the final manuscript.

Funding

The study was supported by the Key Research and Development Project of Ningxia Hui Autonomous Region (2023BEG03046), the Natural Science Foundation of Ningxia Hui Autonomous Region (2022AAC03542) and the Open Project Funding Projects from Ningxia Key Laboratory of Clinical and Pathogenic Microbiology (MKLG-2024-08).

Data availability

The data in this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

In accordance with the Declaration of Helsinki, this retrospective study was permitted by the ethics committee of the General Hospital of Ningxia Medical University, and the requirement to obtain informed written consent was waived.

To protect patients' personal information and maintain the security of General Hospital of Ningxia Medical University's patient information, we are committed to fulfilling our obligation to keep patients' personal information confidential.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]College of Clinical Medicine, Ningxia Medical University, Yinchuan, Ningxia 750004, China
[2]Center of Medical Laboratory, General Hospital of Ningxia Medical University, Yinchuan, China
[3]Ningxia Key Laboratory of Clinical and Pathogenic Microbiology, General Hospital of Ningxia Medical University, Yinchua, China

Received: 10 September 2024 / Accepted: 17 February 2025
Published online: 28 February 2025

References

1. MARTINEZ R M, WOLK DM. Bloodstream Infections [J] Microbiol Spectr, 2016, 4(4).
2. LAUPLAND K B, CHURCH DL. Population-based epidemiology and microbiology of community-onset bloodstream infections [J]. Clin Microbiol Rev. 2014;27(4):647–64.
3. THRIFT A G, THAYABARANATHAN T, HOWARD G, et al. Global stroke statistics [J]. Int J Stroke: Official J Int Stroke Soc. 2017;12(1):13–32.
4. SCHERES L J J, LIJFERING W M, CANNEGIETER SC. Current and future burden of venous thrombosis: not simply predictable [J]. Res Pract Thromb Haemostasis. 2018;2(2):199–208.
5. CONRAD N, JUDGE A, TRAN J, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals [J]. Lancet (London England). 2018;391(10120):572–80.
6. ANDERSON DJ, MOEHRING R W, SLOANE R, et al. Bloodstream infections in community hospitals in the 21st century: a multicenter cohort study [J]. PLoS ONE. 2014;9(3):e91713.
7. CHEN X, ZOU Q, ZHANG W, et al. Clinical features and microbiological characteristics of hospital- and community-onset Escherichia coli bloodstream infection [J]. J Med Microbiol. 2019;68(2):178–87.
8. DAGA A P, KOGA V L, SONCINI J G M et al. Escherichia coli Bloodstream Infections in Patients at a University Hospital: Virulence Factors and Clinical Characteristics [J]. Frontiers in cellular and infection microbiology, 2019, 9(191.
9. BASSETTI M, PECORI D, SIBANI M et al. Epidemiology and treatment of MDR Enterobacteriaceae [J]. 2015, 7(291–316.
10. CANTóN R, GONZáLEZ-ALBA JM, GALáN JC. CTX-M Enzymes: Origin and Diffusion [J]. Frontiers in microbiology, 2012, 3(110.
11. VAN HOEK A H, MEVIUS D, GUERRA B et al. Acquired antibiotic resistance genes: an overview [J]. Frontiers in microbiology, 2011, 2(203.
12. PHAM TD, ZIORA Z M, BLASKOVICH M A J. M. Quinolone antibiotics [J]. 2019, 10(10): 1719-39.
13. KUANG D, ZHANG J, XU X, et al. Emerging high-level ciprofloxacin resistance and molecular basis of resistance in Salmonella enterica from humans, food and animals [J]. Int J Food Microbiol. 2018;280:1–9.
14. HOPKINS K L, DAVIES R H, THRELFALL E J. Mechanisms of quinolone resistance in Escherichia coli and Salmonella: recent developments [J]. Int J Antimicrob Agents. 2005;25(5):358–73.
15. YOSHIDA H, BOGAKI M, NAKAMURA M, et al. Quinolone resistance-determining region in the DNA gyrase gyrA gene of Escherichia coli [J]. Antimicrob Agents Chemother. 1990;34(6):1271–2.

16. MITRA S, MUKHERJEE S, NAHA S et al. Evaluation of co-transfer of plasmid-mediated fluoroquinolone resistance genes and bla(NDM) gene in Enterobacteriaceae causing neonatal septicaemia [J]. Antimicrobial resistance and infection control, 2019, 8(46.
17. VARUGHESE L R, RAJPOOT M. Analytical profiling of mutations in quinolone resistance determining region of gyrA gene among UPEC [J]. PLoS ONE. 2018;13(1):e0190729.
18. REDGRAVE L S, SUTTON S B, WEBBER M A, et al. Fluoroquinolone resistance: mechanisms, impact on bacteria, and role in evolutionary success [J]. Trends Microbiol. 2014;22(8):438–45.
19. RUIZ J. Transferable mechanisms of Quinolone Resistance from 1998 onward [J]. Clin Microbiol Rev, 2019, 32(4).
20. XIAO S, TANG C, ZENG Q et al. Antimicrobial Resistance and Molecular Epidemiology of Escherichia coli From Bloodstream Infection in Shanghai, China, 2016–2019 [J]. Frontiers in medicine, 2021, 8(803837.
21. XIANG G, LAN K, CAI Y et al. Clinical Molecular and Genomic Epidemiology of Morganella morganii in China [J]. Frontiers in microbiology, 2021, 12(744291.
22. JIN Y F EVERETTMJ. Contributions of individual mechanisms to fluoroquinolone resistance in 36 Escherichia coli strains isolated from humans and animals [J]. Antimicrob Agents Chemother. 1996;40(10):2380–6.
23. CLSI I J C W LEWISS, NJ. USA. M100 Performance standards for antimicrobial susceptibility testing [J]. 2022.
24. BLAIR PW, MEHTA R, OPPONG C K, et al. Screening tools for predicting mortality of adults with suspected sepsis: an international sepsis cohort validation study [J]. BMJ open. 2023;13(2):e067840.
25. MOHUS R M, GUSTAD L T, FURBERG A S, et al. Explaining sex differences in risk of bloodstream infections using mediation analysis in the population-based HUNT study in Norway [J]. Sci Rep. 2022;12(1):8436.
26. NAAS T, POIREL L. NORDMANN P. Minor extended-spectrum beta-lactamases [J]. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious diseases, 2008, 14 Suppl 1(42–52.
27. VAN DUIJN P J, DAUTZENBERG M J, OOSTDIJK E A. Recent trends in antibiotic resistance in European ICUs [J]. Curr Opin Crit Care. 2011;17(6):658–65.
28. GUENTHER S, EWERS C. WIELER L H. Extended-Spectrum Beta-Lactamases Producing E. coli in Wildlife, yet Another Form of Environmental Pollution? [J]. Frontiers in microbiology, 2011, 2(246.
29. ZHANG Y, ZHAO C, WANG Q, et al. High prevalence of Hypervirulent Klebsiella pneumoniae infection in China: Geographic distribution, clinical characteristics, and Antimicrobial Resistance [J]. Antimicrob Agents Chemother. 2016;60(10):6115–20.
30. YU Y, JI S, CHEN Y, et al. Resistance of strains producing extended-spectrum beta-lactamases and genotype distribution in China [J]. J Infect. 2007;54(1):53–7.
31. XIA S, FAN X, HUANG Z, et al. Dominance of CTX-M-type extended-spectrum β-lactamase (ESBL)-producing Escherichia coli isolated from patients with community-onset and hospital-onset infection in China [J]. PLoS ONE. 2014;9(7):e100707.
32. STRAHILEVITZ J, JACOBY G A, HOOPER D C, et al. Plasmid-mediated quinolone resistance: a multifaceted threat [J]. Clin Microbiol Rev. 2009;22(4):664–89.
33. VETTING M W, PARK C H, HEGDE SS, et al. Mechanistic and structural analysis of aminoglycoside N-acetyltransferase AAC(6')-Ib and its bifunctional, fluoroquinolone-active AAC(6')-Ib-cr variant [J]. Biochemistry. 2008;47(37):9825–35.
34. FERNáNDEZ-MARTíNEZ M, MIRó E, ORTEGA A, et al. Molecular identification of aminoglycoside-modifying enzymes in clinical isolates of Escherichia coli resistant to amoxicillin/clavulanic acid isolated in Spain [J]. Int J Antimicrob Agents. 2015;46(2):157–63.
35. PALTANSING S, KRAAKMAN M E, RAS JM, et al. Characterization of fluoroquinolone and cephalosporin resistance mechanisms in Enterobacteriaceae isolated in a Dutch teaching hospital reveals the presence of an Escherichia coli ST131 clone with a specific mutation in parE [J]. J Antimicrob Chemother. 2013;68(1):40–5.
36. DAS B, SHAMSUZZAMAN S M, DAS TK. Detection of Quinolone resistance qnr genes and its association with extended spectrum β-lactamase and AmpC β-lactamase genes in qnr positive Enterobacteriaceae in Bangladesh [J]. Mymensingh Med Journal: MMJ. 2024;33(1):183–91.
37. DALHOFF A. Global fluoroquinolone resistance epidemiology and implictions for clinical use [J]. Interdisciplinary perspectives on infectious diseases; 2012. 2012(976273.
38. COULTHURST SJ, BARNARD A M, SALMOND GP. Regulation and biosynthesis of carbapenem antibiotics in bacteria [J]. Nat Rev Microbiol. 2005;3(4):295–306.
39. CORNAGLIA G, GIAMARELLOU H, ROSSOLINI GM. Metallo-β-lactamases: a last frontier for β-lactams? [J]. Lancet Infect Dis. 2011;11(5):381–93.
40. ZHANEL G G, LAWRENCE C K, ADAM H, et al. Imipenem-Relebactam and Meropenem-Vaborbactam: two Novel Carbapenem-β-Lactamase inhibitor combinations [J]. Drugs. 2018;78(1):65–98.
41. FERNANDES R, AMADOR P, PRUDêNCIO CJR et al. β-Lactams: chemical structure, mode of action and mechanisms of resistance [J]. 2013, 24(1): 7–17.
42. ALMAGHRABI R, CLANCY C J, DOI Y, et al. Carbapenem-resistant Klebsiella pneumoniae strains exhibit diversity in aminoglycoside-modifying enzymes, which exert differing effects on plazomicin and other agents [J]. Antimicrob Agents Chemother. 2014;58(8):4443–51.
43. NORDMANN P, DORTET L. Carbapenem resistance in Enterobacteriaceae: here is the storm! [J]. Trends Mol Med. 2012;18(5):263–72.
44. QUEENAN A M BUSHK. Carbapenemases: the versatile beta-lactamases [J]. Clin Microbiol Rev, 2007, 20(3): 440– 58, table of contents.
45. DI TELLA D, TAMBURRO M, GUERRIZIO G, et al. Molecular Epidemiological insights into Colistin-resistant and carbapenemases-producing clinical Klebsiella pneumoniae isolates [J]. Infect drug Resist. 2019;12:3783–95.
46. YAGHOUBI S, ZEKIY A O KRUTOVAM, et al. Tigecycline antibacterial activity, clinical effectiveness, and mechanisms and epidemiology of resistance: narrative review [J]. Eur J Clin Microbiol Infect Diseases: Official Publication Eur Soc Clin Microbiol. 2022;41(7):1003–22.
47. VELKOV T, THOMPSON P E, NATION R L, et al. Structure–activity relationships of polymyxin antibiotics [J]. J Med Chem. 2010;53(5):1898–916.
48. LIPWORTH S, VIHTA K D, CHAU K, et al. Ten-year longitudinal molecular epidemiology study of Escherichia coli and Klebsiella species bloodstream infections in Oxfordshire, UK [J]. Genome Med. 2021;13(1):144.
49. PARAMITA R I, NELWAN E J, FADILAH F, et al. Genome-based characterization of Escherichia coli causing bloodstream infection through next-generation sequencing [J]. PLoS ONE. 2020;15(12):e0244358.
50. NAMAEI M H, YOUSEFI M, ZIAEE M et al. First Report of Prevalence of CTX-M-15-Producing Escherichia coli O25b/ST131 from Iran [J]. Microbial drug resistance (Larchmont, NY), 2017, 23(7): 879–84.
51. HOJABRI Z, DARABI N, ARAB M, et al. Clonal diversity, virulence genes content and subclone status of Escherichia coli sequence type 131: comparative analysis of E. Coli ST131 and non-ST131 isolates from Iran [J]. BMC Microbiol. 2019;19(1):117.
52. MATSUMURA Y, YAMAMOTO M, NAGAO M, et al. Association of fluoroquinolone resistance, virulence genes, and IncF plasmids with extended-spectrum-β-lactamase-producing Escherichia coli sequence type 131 (ST131) and ST405 clonal groups [J]. Antimicrob Agents Chemother. 2013;57(10):4736–42.
53. DE SOUZA DA-SILVA A P, DE SOUSA V S, DE ARAúJO LONGO L G et al. Prevalence of fluoroquinolone-resistant and broad-spectrum cephalosporin-resistant community-acquired urinary tract infections in Rio de Janeiro: Impact of Escherichia coli genotypes ST69 and ST131 [J]. Infection, genetics and evolution: journal of molecular epidemiology and evolutionary genetics in infectious diseases, 2020, 85(104452.
54. LEE M Y, CHOI H J, CHOI J Y, et al. Dissemination of ST131 and ST393 community-onset, ciprofloxacin-resistant Escherichia coli clones causing urinary tract infections in Korea [J]. J Infect. 2010;60(2):146–53.
55. RECHKINA TCHESNOKOVAVL. Rapid and extensive expansion in the United States of a New Multidrug-resistant Escherichia coli Clonal Group, sequence type 1193 [J]. Clin Infect Diseases: Official Publication Infect Dis Soc Am. 2019;68(2):334–7.
56. WU J, LAN F, LU Y et al. Molecular Characteristics of ST1193 Clone among Phylogenetic Group B2 Non-ST131 Fluoroquinolone-Resistant Escherichia coli [J]. Frontiers in microbiology, 2017, 8(2294.

Publisher's note